REMARKS

Favorable reconsideration is requested in view of the foregoing amendments and the following remarks.

I. Claim Status & Amendments

Claims 7-16 were pending in this application when last examined and stand rejected.

Claim 7 is amended to incorporate the subject matter of claim 8, which has been cancelled. Claim 10 is amended to depend on claim 13. Claim 13 is amended to incorporate the subject matter of general formula I as previously defined in claim 7 (before being combined with claim 8). Other minor editorial revisions have been made to the claims to better conform to U.S. claim form and practice. Such revisions are non-substantive and not intended to narrow the scope of protection. No new matter has been added.

Claims 8, 9, 11, and 14-16 have been cancelled without prejudice or disclaimer thereto. Applicants reserve the right to file a continuation or divisional application on any cancelled subject matter.

Claims 7, 10, 12, and 13 are pending upon entry of this amendment.

Applicants note the amended claims do not present any new issues for consideration and/or search as they incorporate subject matter already considered by the Office.

Accordingly, if the next Office Action on the merits includes a new ground of rejection of one or more claims, the Action must be non-final.

II. Indefiniteness and 101 Patentable Subject Matter Rejections

Claim 9 was rejected under 35 U.S.C. § 112, second paragraph, and under 35 U.S.C. § 101, as being an improper method claim for not including any steps for the claimed method.

The present amendment cancels claim 9, thereby rendering the rejections moot.

III. Double Patenting and Prior Art Rejections

Claims 7, 8, and 10-16 were rejected on the ground of nonstatutory obviousness-type double patenting as being obvious over claims 1-5 of US 5,912,242 for the reasons on page 4 of the Office Action. Claims 7, 8, and 10-16 were rejected under 35 U.S.C. § 102(b) as anticipated by Peverello et al. (WO 97/05111) for the reasons on page 5. Claim 7 was rejected under 35 U.S.C. § 102(b) as anticipated by Suzuki et al. (JP 01204073A) for the reasons on page 5.

It is respectfully submitted that the present amendment overcomes these rejections by amending the claims in manner believed to exclude the known compounds and to remove

overlapping subject. Withdrawal of the rejections is requested.

IV. Enablement Rejection

Claims 12-16 were rejected under 35 U.S.C. § 112, first paragraph, on the basis that the specification is enabled for compounds and a method of treating pain and other disorders such as inflammatory pain, hypertension, arrhythmias, and diabetes, it is not enabled for treating the generic classes of diseases, such as cognitive disorders, inflammation, gastrointestinal tract disorders, and disorders of the genitor urinary tract for the reasons on pages 5-9 of the Office Action.

This rejection is respectfully traversed.

The test of enablement is whether one reasonably skilled in the art could make or use the invention based on the disclosure in the specification coupled with the knowledge in the art without undue experimentation. The fact that experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation. M.P.E.P., Eighth Ed., Rev. 6 (September 2007) at § 2164.01 and *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). The test of enablement is not whether any experimentation is necessary, but whether, if experimentation

is necessary, it is undue. In fact, the test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification provides reasonable guidance with respect to the direction in which the experimentation should proceed.

In the instant case, it is respectfully submitted that the disclosure provides sufficient guidance to enable treating the scope of the conditions recited in claim 13.

To start, as acknowledged at page 6 of the Office Action, the specification discloses use of a compound according to formula I for the treatment of diseases that are modulated by the calcium and/or sodium channel. Moreover, the specification clearly describes in detail the mechanism of action involving calcium and/or sodium channels as related to the disease conditions recited in the claims.

In this regard, the specification (see paragraph [011] of the patent application publication no. 20070135410) disclose the important role sodium channels play in the neuronal network by transmitting electrical impulses rapidly throughout cells and cell networks, thereby coordinating higher processes ranging from locomotion to cognition.

In paragraphs [0012-0013], it is disclosed that neuronal sodium channel blockers have found application with their use in the treatment of epilepsy (phenyloin and carbamazepine), bipolar disorder (lamotrigine), preventing

neurodegeneration, and in reducing neuropathic pain. Various anti-epileptic drugs that stabilize neuronal excitability are effective in neuropathic pain (gabapentin), and that an increase in sodium channel expression or activity has also been observed in several models of inflammatory pain, suggesting a role of sodium channels in inflammatory pain. In paragraphs [0014 to 0016], it discloses that findings indicate that compounds with sodium and/or calcium channel blockade have a high therapeutic potential in preventing, alleviating and curing a wide range of pathologies, including neurological, psychiatric, cardiovascular, urologic, metabolic and gastrointestinal diseases, where the ntoed mechanisms have been described as playing a pathological role.

The invention is related to 3-aminopyrrolidone derivatives and analogues of the following general formula I and pharmaceutically acceptable salts thereof, that are active as sodium and/or calcium channel modulators and therefore useful in treating a wide range of conditions including neurological, psychiatric, cardiovascular, inflammatory, ophthalmic, urologic, metabolic and gastrointestinal diseases, where the mechanisms described in the specification have been shown to play a pathological role.

Nonetheless, on page 7, the Office Action contends that "the invention is highly unpredictable since one skilled in the art would recognize that a group of compounds and

compositions may act as the calcium and/or sodium channel blockers that have involvement (either directly or peripherally) within the mechanism of action) in certain diseases; but, it does not mean that the same group of compounds and compositions may treat all diseases associated with the calcium and/or sodium ion channels."

Applicants respectfully disagree.

Contrary to the Office's position, the claims are not directed to treating all diseases associated with the calcium and/or sodium ion channels. Instead, the method claims are directed to treating the specific conditions of "pain, migraine, cognitive disorders, inflammation, gastrointestinal tract disorders, disorders of the genitor urinary tract, ophthalmic diseases or obesity" as recited in claim 13. Thus, there is no need to demonstrate efficacy for any and all diseases associated with the calcium and/or sodium ion channels.

As to the pharmaceutical composition of claim 12, the Office has already acknowledged that the specification is enabled for compounds and a method of treating pain and other disorders such as inflammatory pain, hypertension, arrhythmias, and diabetes. This statement alone acknowledges the enabling support for a pharmaceutical composition. In other words, since the Office has acknowledged that the specification is enabling for treating at least one condition,

the specification supports a claim to a pharmaceutical composition.

Also, contrary to the Office's position, the specification discloses effective dosage ranges suitable to achieve effectiveness. See for instance, paragraph [0187] of the published application no. 2007-0135410A1, which discloses:

> As a consequence of these mechanisms the compounds of the invention are active in vivo when orally administered in the range of 0.1 to 100 mg/kg in animal models such as the formalin model of persistent pain and the carragenan model of inflammation.

See also paragraphs [202] to [213], wherein dosages and routes of administration are discussed in detail. For instance, paragraph [213] discloses:

> The pharmaceutical compositions comprising the 3-aminopyrrolidone derivatives of formula I as above defined will contain, per dosage unit, e.g., capsule, tablet, powder injection, teaspoonful, suppository and the like from about 0.1 to about 500 mg of the active ingredient most preferably from 1 to 10 mg.

Further, as acknowledged by Office, the specification provides *in vitro* and *in vivo* experiments showing enablement for compounds and methods of treating at least pain and other disorders such as inflammatory pain, hypertension, arrhythmias, and diabetes.

In this regard, the specification describes in detail the disease conditions mediated by inhibition of voltage gated sodium channels and/or voltage gated calcium

channels. Further, the specification provides *in vitro* data showing inhibition of calcium and sodium channels by compounds of the present application. See, for instance, the "Calcium Influx assay" of Example 10 in paragraphs [240] to [247], which studied and demonstrated inhibition of calcium channels by representative compounds of the invention as compared to a reference standard, ralfinamide. See, also, the "Electrophysiological assay" of Example 11 in paragraphs [248] to [266], which results are predictive of a good analgesic effect in *in vivo* pain models. See, also, the *in vivo* animal studies in Examples 12 and 13 on page 32, which also disclose effective dosages for treatment.

Furthermore, Applicants are submitting herewith a Rule 132 Declaration by Dr. Patricia Salvati as further evidence that the specification is enabled for the full scope of treatment recited in the claims. The Rule 132 Declaration discusses the *in vitro* and *in vivo* data in the disclosure and presents data as to the effectiveness of the claimed methods. It is believed that this Declaration further substantiates that the specification is enabled for the full scope of the claims.

Therefore, it is believed that the skilled artisan, upon reading this disclosure, the working examples, and in view of the knowledge in the art, could extrapolate the appropriate dosages from the ranges and examples in the

specification to successively treat subjects for the full scope of the recited conditions without undue experimentation. Thus, withdrawal of the rejection is requested.

V. Conclusion

Having addressed all the outstanding issues, the amendment is believed to be fully responsive. In view of the above, it is respectfully submitted that the application is in condition for allowance and notice to that effect is hereby requested. If the Examiner has any comments or proposals for expediting prosecution, please contact the undersigned attorney at the telephone number below.

The Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 25-0120 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17.

Respectfully submitted,

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JFW/ml

APPENDIX:

The Appendix includes the following item(s):

☒ – a 37 CFR 1.132 Declaration